AUSTRALIAN GROUP ON ANTIMICROBIAL RESISTANCE

Australian Enterococcus Surveillance Outcome Program (AESOP)

Bloodstream Infection Report

2022 Final Report

July 2023

Contents

Key findings

Enterococcus species

- Between 1 January to 31 December 2022 a total of 1,535 episodes of enterococcal bacteraemia were reported; the majority (92.8%) were caused by *Enterococcus faecalis* or *Enterococcus faecium.*
- Twenty-nine *Enterococcus lactis* were identified. Prior to 2022 this species was identified as *E. faecium*.
- Approximately two thirds (67.0%) of *E. faecalis* bacteraemias were community-onset (CO), whilst in *E. faecium* bacteraemias only 25.6% were CO.
- The most frequent source of bacteraemia or clinical manifestation for *E. faecalis* was urinary tract infection (22.5%); for *E. faecium*, it was febrile neutropenia (19.8%).
- The combined 30-day all-cause mortality for *E. faecalis* and *E. faecium* was 21.3%.
- There was significant difference in 30-day all-cause mortality between *E. faecalis* (17.2%) and *E. faecium* (26.4%) *P* <0.01 and between vancomycin-resistant and vancomycin-susceptible *E. faecium* episodes (34.5% and 19.1% respectively) *P* <0.01
- The length of stay in hospital following enterococcal bacteraemia was more than 30 days for 22.3% of patients.
- For the bloodstream infections caused by *E. faecium*, 46.9% were phenotypically vancomycin resistant.
- In 2022, 47.7% of *E. faecium* harboured *vanA* and/or *vanB* genes (*vanA* 13.0%, *vanB* 34.7%). In 2021, 39.6% of *E. faecium* harboured *vanA* and/or *vanB* genes.
- For the vancomycin-resistant *E. faecium* (VREfm) bacteraemias, 25.6% were due to *vanA*-harbouring isolates. *vanA* was the dominant genotype in New South Wales.
- There were 62 *E. faecium* multi-locus sequence types (STs), of which ST17, ST78, ST1424, ST796, ST80, ST1421, ST555 and ST117 were the most frequently identified.
- *vanA* genes were detected in six STs, and *vanB* genes were detected in 12 STs. The clonal diversity of *E. faecium* harbouring *van* genes varied across Australia.
- In 2022, for rates of resistance to vancomycin in *E. faecium,* compared to the European Antimicrobial Resistance Surveillance Network (EARS-Net) countries, Australia ranked fourth highest. From 2019 to 2021, Australia has ranked fourth, tenth and eighth respectively.
- Two linezolid-resistant *E. faecium* from Victoria were confirmed in 2022. Both harboured the G2576T 23S rRNA mutation. One isolate with a linezolid MIC of >256 mg/L was ST2217, vancomycin resistant and harboured the *vanB* gene. The second isolate with a linezolid MIC of 8 mg/L was ST1424 and vancomycin susceptible.
- Two daptomycin-resistant isolates from NSW, one *E. faecalis* and one *E. faecium* were confirmed. The *E. faecalis* with a daptomycin MIC of 8 mg/L was ST16 and harboured the F478L GdpD mutation. The *E. faecium* with a daptomycin MIC of 24 mg/L was ST78 and harboured the A20D Cls mutation. The *E. faecium* was also vancomycin-resistant and harboured the *vanB* gene.

Implications of key findings for health care

When interpreting the Australian Group on Antimicrobial Resistance (AGAR) data, it is important to consider changes in surveillance coverage between 2013 and 2022. AGAR has increased the number of hospitals from 26 in 2013 to 55 in 2022. In addition, the relative distribution of sites has changed with the addition of three more paediatric facilities in 2017, one in 2019, another in 2020 and 2021 (a total of seven paediatric hospitals) and the inclusion of hospitals from north-west regional Western Australia from 2015.

Several themes are discussed below which have implications for the delivery of health care services and the safety of care provided to patients. These have been identified from the analyses of AGAR data.

Changing patterns in *Enterococcus* species

The number of enterococcal bacteraemia episodes identified by AGAR (for hospitals participating in both years) increased in 2022 compared to 2021 from 1,300 to 1,402 (up 7.9%). The increase was mostly in the number of *E. faecium* (493 vs 539, up 9.3%) rather than *E. faecalis* episodes (705 vs 707, up 0.3%).

The number of VREfm isolates increased from 198 in 2021 to 285 in 2022. There was an increase in overall vancomycin resistance rates in *E. faecium* from 40.2% to 46.9%. There was an increase in VREfm as a proportion of all enterococcal isolates from 15.2% to 18.6%. The overall contribution of *vanA* and *vanB* genes to VREfm varied according to jurisdiction. *vanA*-harbouring VREfm were dominant in New South Wales, whilst *vanB*-harbouring VREfm were dominant in the remainder of Australia with the exception of Queensland where they were detected in equal numbers.

Optimising all VREfm prevention and infection control mechanisms will be required to respond effectively to resistance in *E. faecium* in Australia.

Epidemiology of clinical manifestations

Urinary tract infection remains the most common manifestation associated with *E. faecalis* blood stream infection. In 2022 febrile neutropenia and intra-abdominal infection other than biliary tract were the most common clinical manifestations associated with *E. faecium* bacteraemias.

Variation across states and territories

Rates of vancomycin resistance in *E. faecium* ranged from 13.0% in Queensland to 65.0% in South Australia. Teicoplanin resistance ranged from 7.3% in Queensland to 22.1% in New South Wales.

Appropriate adaptation of national treatment guidelines should be considered in order to minimise the use of broad-spectrum antimicrobials whilst balancing delivery of the most appropriate antimicrobial for severe infections.

Variations between hospital and community settings

E. faecium was more commonly hospital-onset (74.4%) compared to *E. faecalis* (25.6%) hospital-onset. Where susceptibility results were known, VREfm bacteraemia accounted for 7.3% (55/758) of all community-onset enterococcal bacteraemia, compared to 30.3% (230/759) in hospital-onset disease.

These variations have implications for choice of empiric antimicrobial therapy and guidelines in community- versus hospital-onset infections, and accounting for infections in aged care home residents (which are included in the community-onset group in the AGAR data, but not distinguished as such in this report).

1. Background and objectives

AGAR commenced in 1985 and was established to collect national data on antimicrobial resistance (AMR) in bacteria causing important and life-threatening infections.

Historically, the main focus of AGAR was AMR in Staphylococcus aureus. The scope broadened over time to include surveillance studies on Escherichia coli, Enterobacter species, Klebsiella species, Haemophilus influenzae, Streptococcus pneumoniae and Enterococcus species. AGAR now concentrates on three groups of pathogens within the programs: Australian Staphylococcus aureus Surveillance Outcome Program (ASSOP), Australian Enterococcal Surveillance Outcome Program (AESOP) and the Gram-Negative Surveillance Outcome Program (GnSOP).

AGAR's focus on bacteraemia allows examination of laboratory-confirmed, invasive infections and comparison of rates over time for hospitals, states and territories. AGAR compares Australian data with EARS-Net, enabling benchmarking and trend projections. AGAR has collected ongoing data on the prevalence of AMR in Australia over a long period using standardised methods

The 2022 AESOP report presents analyses of AMR associated with episodes of enterococcal bacteraemia (blood stream infection) that were reported by 33 participating Australian public and private laboratories servicing 55 hospitals across Australia in 2022.

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The 55 hospitals across Australia that currently contribute to AGAR, including five private hospitals, are listed in Table 1. In 2022, three additional hospitals, (two from NSW and one from Queensland), contributed data.

AGAR publishes detailed annual reports on each program on its website (www.agargroup.org.au), and in the Communicable Diseases Intelligence (CDI) journal.

AGAR is part of the Antimicrobial Use and Resistance in Australia (AURA) surveillance system funded by the Australian Government Department of Health and Aged Care.

Table 1: Hospitals that contributed to AGAR, by state and territory, AGAR, 2022

State or territory	Hospital
New South Wales	Children's Hospital Westmead
	Concord Repatriation General Hospital
	Gosford Hospital
	John Hunter Hospital
	Liverpool Hospital
	Nepean Hospital
	Prince of Wales Hospital
	Royal North Shore Hospital
	Royal Prince Alfred Hospital
	St Vincent's Hospital, Sydney*
	Sydney Children's Hospital
	Westmead Hospital
	Wollongong Hospital
Victoria	Alfred Hospital
	Austin Hospital (Austin Health)
	Monash Children's Hospital†
	Monash Medical Centre (Dandenong Hospital)†
	Monash Medical Centre (Monash Health)
	Royal Melbourne Hospital
	Royal Women's and Children's Hospital
	St Vincent's Hospital*
Queensland	Gold Coast Hospital
	Greenslopes Private Hospital# ††
	Mater Hospital, Townsville# ††
	Prince Charles Hospital§
	Princess Alexandra Hospital§
	Queensland Children's Hospital§
	Royal Brisbane and Women's Hospital
South Australia	Flinders Medical Centre
	Royal Adelaide Hospital
	Women's and Children's Hospital*
Western Australia	Fiona Stanley Hospital
	Joondalup Hospital*
	North-west regional Western Australia (Broome, Derby, Fitzroy Crossing, Halls Creek, Karratha, Kununurra, Newman, Onslow, Paraburdoo, Port Hedland, Roebourne, Tom Price, and Wyndham)§§
	Perth Children's Hospital§§
	Royal Perth Hospital##
	Sir Charles Gairdner Hospital
	St John of God Hospital, Murdoch††
Tasmania	Launceston General Hospital
	Royal Hobart Hospital
Northern Territory	Alice Springs Hospital
	Royal Darwin Hospital
Australian Capital Territory	Canberra Hospital

*	Public/private hospital
†	Microbiology services provided by Monash Medical Centre (Monash Health)
§	Microbiology services provided by Pathology Queensland Central Laboratory
#	Microbiology services provided by Sullivan Nicolaides Pathology
**	Microbiology services provided by SA Pathology, Royal Adelaide Hospital
††	Private hospital
§§	Microbiology services provided by PathWest Laboratory Medicine WA, Sir Charles Gairdner Hospital
##	Microbiology services provided by PathWest Laboratory Medicine WA, Fiona Stanley Hospital

1.1. Australian Enterococcal Surveillance Outcome Program

Globally, enterococci are thought to account for approximately 10% of all bacteraemias, and in North America and Europe are the fourth and fifth leading causes of sepsis respectively.[1, 2] In the 1970s healthcare-associated enterococcal infections were primarily due to *Enterococcus faecalis*, however subsequently there has been a steady increase in prevalence of *E. faecium* nosocomial infections.[3-5] Worldwide, the increase in nosocomial *E. faecium* infections has primarily been due to the expansion of polyclonal hospital-adapted clonal complex (CC) 17 isolates. While innately resistant to many classes of antimicrobials, *E. faecium* CC17 has demonstrated a remarkable capacity to evolve new antimicrobial resistances. In 2009, the Infectious Diseases Society of America highlighted *E. faecium* as one of the key problem bacteria or ESKAPE (*E. faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Enterobacter* species) pathogens requiring new therapies.[6]

AGAR began surveillance of antimicrobial resistance in *Enterococcus* species in 1995.[7] In 2011, AGAR commenced the Australian Enterococcal Sepsis Outcome Program (AESOP).[8] The term “Sepsis” in the program was changed in 2021 to “Surveillance” to better reflect AGAR’s surveillance of episodes of bacteraemia rather than sepsis.

In order to provide data to support improved antimicrobial prescribing and patient care, the objective of AESOP 2022 was to determine the proportion of *E. faecalis* and *E. faecium* bacteraemia isolates demonstrating antimicrobial resistance with particular emphasis on:

- Assessing susceptibility to ampicillin
- Assessing susceptibility to glycopeptides, and the associated resistance genes
- Monitoring the molecular epidemiology of *E. faecium.*

2. Summary of methods

Fifty-five institutions, in each state and territory of Australia, were enrolled in the 2022 AGAR programs. The AGAR laboratories collected all isolates from unique patient episodes of bacteraemia from 1 January 2022 to 31 December 2022. Approval to conduct the prospective data collection, including de-identified demographic data, was given by the research ethics committees associated with each participating hospital.

In patients with more than one isolate, a new episode was defined as a new positive blood culture more than two weeks after the initial positive culture. An episode was defined as community onset if the first positive blood culture was collected 48 hours or less after admission, and as hospital onset if collected more than 48 hours after admission.

AGAR meets the data security requirements of the AURA surveillance system. These arrangements ensure that data conform to appropriate standards of data management and quality, and that data are used in accordance with appropriate approvals. The Australia Society for Antimicrobials (ASA), as data custodian for AGAR data, is responsible for:

- Approving access to, and use of, AGAR data
- Ensuring that AGAR data are protected from unauthorised access, alteration, or loss
- Ensuring compliance with relevant legislation and policies regarding administration, quality assurance, and data access and release.

2.1. Data fields

Laboratory data collected for each episode included an accession number, the date the blood culture was collected, the organism isolated (genus and species), and the antimicrobial susceptibility test results (minimum inhibitory concentrations) for each species. The patient's date of birth, sex and postcode of residence were also provided. If the patient was admitted to hospital, the dates of admission and discharge were recorded. Depending on the level of participation, limited clinical and outcome data were also provided. The data included the principal clinical manifestation, device related infection (yes or no) and the outcome (died, all-cause or survived) at seven and 30 days (see Appendix A).

2.2. Species identification

Isolates were identified to species level, if possible, using the routine method for each institution. This included the Vitek® 2 and BD Phoenix™ automated microbiology systems, and if available, matrix assisted laser desorption ionization-time of flight (MALDI-TOF) mass spectrometry (Bruker MALDI biotyper® or Vitek® MS).

2.3. Susceptibility testing

Susceptibility testing of isolates is described in Appendix B. The analysis used breakpoints from the Clinical and Laboratory Standards Institute (CLSI) M100–Ed33[9] and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) v13.1.[10]

2.4. PCR screening and whole genome sequencing

For all *E. faecium* received, whole genome sequencing (WGS) was performed by the Antimicrobial Resistance and Infectious Diseases (AMRID) Research Laboratory at Murdoch University on the Illumina NextSeq™ 500 platform. The multilocus sequence type (ST) was determined using the PubMLST website and *van* genes were identified using nucleotide sequences from the NCBI database and a BLAST interface.[11]

2.5. Statistical Analysis

Confidence intervals for proportions, Fisher's exact test for categorical variables, and chi-squared test for trend were calculated, if appropriate, using MedCalc for Windows, version 19.7.4 (MedCalc Software, Ostend Belgium).

3. Results

3.1. Isolates recovered

There were 1,297 episodes of enterococcal bacteraemia. *E. faecalis* and *E. faecium* accounted for 94.4% of all enterococcal isolates (Table 2).

Table 2: Number of each enterococcal species recovered, by state and territory, AGAR, 2022

Organism	NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Total *Enterococcus* species	494	384	161	123	207	81	33	52	1,535
*Enterococcus faecalis**	249	180	92	75	118	51	14	33	812
vancomycin-resistant, percent	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
vancomycin-susceptible, percent	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
*Enterococcus faecium**	215	178	54	41	71	23	14	17	613
vancomycin-resistant, percent	49.3	62.4	13.0	65.0	16.9	34.8	57.1	52.9	46.9
vancomycin-susceptible, percent	50.7	37.6	87.0	35.0	83.1	65.2	42.9	47.1	53.1
Other enterococcal species	30	26	15	7	18	7	5	2	110
Enterococcus lactis†	9	7	4	1	3	2	2	1	29
Enterococcus casseliflavus	4	4	2	3	5	2	1		21
Enterococcus gallinarum	3	6	5	1	2				17
Enterococcus avium	4	4	2		3	2		1	16
Enterococcus raffinosus	6	2	1	2	1		1		13
Enterococcus hirae	1	1	1		2				5
Enterococcus durans	1	1				1	1		4
Enterococcus gilvus					2				2
Enterococcus dispar		1							1
Enterococcus cecorum	1								1
Enterococcus species	1								1

* Vancomycin susceptibilities were not available for five *E. faecalis* and five *E. faecium*
† Prior to 2022 classified as *E. faecium*

NSW = New South Wales, VIC = Victoria, QLD = Queensland, SA = South Australia, WA = Western Australia, Tas = Tasmania, NT = Northern Territory, ACT = Australian Capital Territory

3.2. Place of onset of bacteraemia

Overall 1,511 (98.4%) patients with enterococcal bacteraemia were admitted to hospital.

Information on place of onset of bacteraemia was available for all *Enterococcus* species episodes (Table 3).

Episodes involving *E. faecalis* and 'other' *Enterococcus* species were predominantly community onset (*E. faecalis* [67.0%, 95% CI: 63.7-70.2] and other *Enterococcus spp.* [60.0%, CI: 56.4-74.7]). However, *E. faecium* episodes were predominantly hospital onset (74.4%; 95% CI: 70.5-77.8). The proportion of *E. faecalis* that were community onset was significantly lower amongst children (43.3%, 29/67) than adults (69.1%, 515/745) *P* <0.01.

Table 3: Species recovered, by place of onset, AGAR, 2022

Organism	Community onset % (*n*)	Hospital onset % (*n*)	Total
Enterococcus species	50.0 (767)	50.0 (768)	1,535
Enterococcus faecalis	67.0 (544)	33.0 (268)	812
vancomycin-resistant	–* (0)	–* (0)	0
vancomycin-susceptible	67.0 (541)	33.0 (266)	807
Enterococcus faecium	25.6 (157)	74.4 (456)	613
vancomycin-resistant	19.3 (55)	80.7 (230)	285
vancomycin-susceptible	31.3 (101)	68.7 (222)	323
Other *Enterococcus* species (*n* = 11)	60.0 (66)	40.0 (44)	110

* Insufficient numbers (<10) to calculate percentage

Note: Vancomycin susceptibilities were not available for five *E. faecalis* (three community-onset, two hospital-onset) and five *E. faecium* (one community-onset, four hospital onset)

3.3. Onset versus 30-day all-cause mortality

Information on 30-day all-cause mortality, when place of onset was known, was available for 1,281 (83.5%) enterococcal bacteraemia episodes (Table 4).

The 30-day all-cause mortality for *Enterococcus* species was significantly lower amongst children (3.9% 3/77) compared to adults (22.3%, 268/1,204) ($P < 0.01$). There was a significant difference in the 30-day all-cause mortality between *E. faecium* (26.9% 141/524) and *E. faecalis* (17.2%, 114/664) ($P < 0.01$) and between vancomycin-resistant (34.4%, 88/256) and vancomycin-susceptible (19.7%, 52/264) *E. faecium* episodes ($P < 0.01$).

Table 4: Onset setting and 30-day all-cause mortality (blood culture isolates), AGAR, 2022

	Community onset		Hospital onset		Total	
Organism	Number	Deaths % (*n*)	Number	Deaths % (*n*)	Number	Deaths % (*n*)
Enterococcus species	634	19.1 (121)	647	23.2 (150)	1,281	21.2 (271)
Enterococcus faecalis	449	16.3 (73)	215	19.1 (41)	664	17.2 (114)
vancomycin-resistant	0	–* (0)	0	–* (0)	0	–* (0)
vancomycin-susceptible	448	16.3 (73)	214	19.2 (41)	662	17.2 (114)
Enterococcus faecium	131	30.5 (40)	393	25.7 (101)	524	26.9 (141)
vancomycin-resistant	49	40.8 (20)	207	32.9 (68)	256	34.4 (88)
vancomycin-susceptible	81	24.7 (20)	183	17.5 (32)	264	19.7 (52)
Other enterococcal species (*n* = 10)	54	14.8 (8)	39	20.5 (8)	93	17.2 (16)

* Insufficient numbers (<10) to calculate percentage

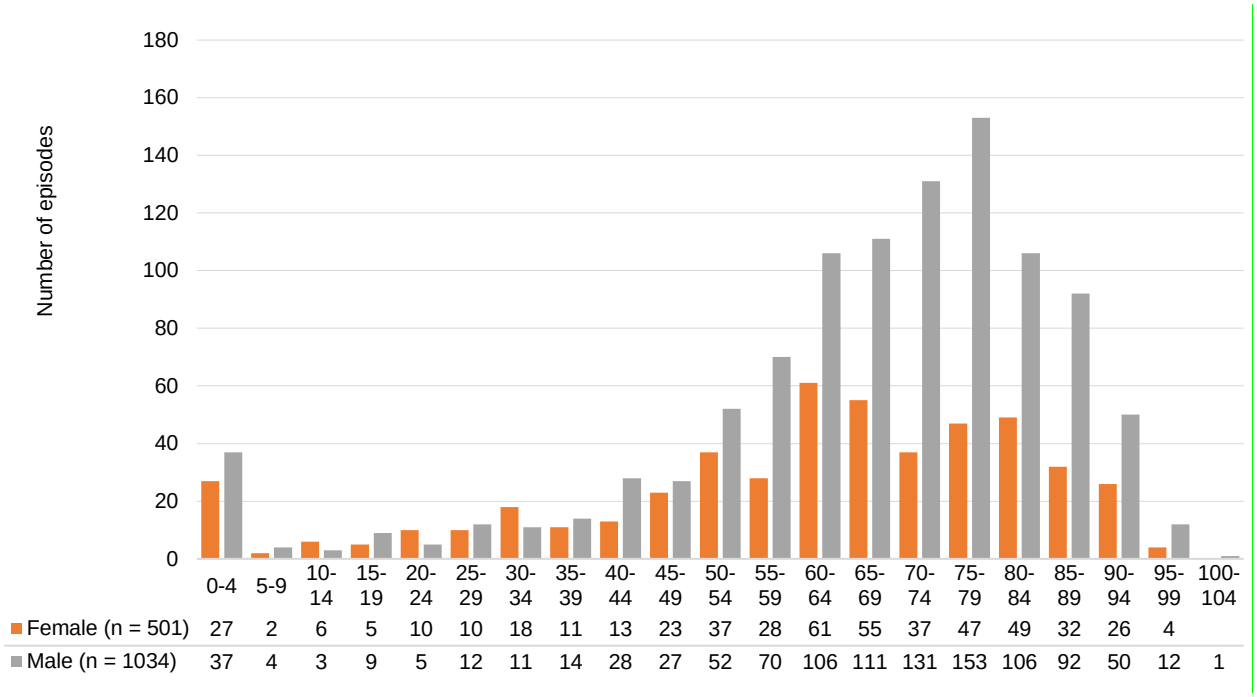
Note: Vancomycin susceptibilities were not available for two *E. faecalis* (one community-onset and one hospital-onset) and four *E. faecium* (one community-onset and four hospital-onset).

3.4. Patient age and sex

Age and sex were available for all patients. The proportion of males was 67.4%.

Increasing age was a surrogate risk factor for bacteraemia (Figure 1); only 12.0% of enterococcal episodes were in patients aged less than 40 years. The proportion of patients aged 0–19 years was 6.1% (*n* = 93).

Figure 1: Number of episodes of bacteraemia due to *Enterococcus* species, by patient age group and sex, AGAR, 2022.



3.5. Principal clinical manifestation

The principal clinical manifestations, which represent the most likely primary site or source for the origin of the blood stream infection, are described below.

The principal clinical manifestation was known for 1,444 (94.1%) patient episodes of enterococcal bacteraemia. Overall, the most frequent principal clinical manifestations were those with urinary tract infection (14.2%), biliary tract infection (14.0%) and those with no identifiable focus (13.6%) (Table 5). There was a significant gender difference in terms of principal clinical manifestation for urinary tract infections.

Of the hospital-onset episodes where data were available, the most frequent principal clinical manifestations were device related infections without metastatic focus (18.6%) and febrile neutropenia (17.1%). Of the community-onset episodes where data were available, the most frequent principal clinical manifestation was urinary tract infection (20.6%) (data not shown).

The principal manifestation was known for 1,340 of the 1,425 (94.0%) *E. faecalis* and *E. faecium* episodes (Table 6). The most common clinical manifestation for *E. faecalis* was urinary tract infection (22.5%), whereas for *E. faecium* it was febrile neutropenia (19.8%) and intra-abdominal infection (18.3%). Significant differences were seen between *E. faecalis* and *E. faecium* for a number of clinical manifestations.

Table 5: Principal clinical manifestation for enterococcal bacteraemia, by patient sex, AGAR, 2022

Principal clinical manifestation	Female % (*n*)	Male % (*n*)	Total % (*n*)	Significance*
Urinary tract infection	8.8 (42)	16.9 (163)	14.2 (205)	<0.01
Biliary tract infection (including cholangitis)	16.1 (77)	12.9 (125)	14.0 (202)	ns
No identifiable focus	14.0 (67)	13.4 (130)	13.6 (197)	ns
Intra-abdominal infection other than biliary tract	14.5 (69)	12.8 (124)	13.4 (193)	ns
Device-related infection without metastatic focus	13.0 (62)	11.7 (113)	12.1 (175)	ns
Febrile neutropenia	10.5 (50)	9.2 (89)	9.6 (139)	ns
Other clinical syndrome	9.0 (43)	8.8 (85)	8.9 (128)	ns
Endocarditis left-sided	6.3 (30)	8.1 (78)	7.5 (108)	ns
Skin and skin structure infection	2.3 (11)	2.2 (21)	2.2 (32)	ns
Osteomyelitis/septic arthritis	2.1 (10)	1.6 (15)	1.7 (25)	ns
Device-related infection with metastatic focus	1.9 (9)	1.4 (14)	1.6 (23)	ns
Endocarditis right-sided	1.5 (7)	1.0 (10)	1.2 (17)	ns
Total	477	967	1,444	

ns = not significant

* Fisher's exact test for difference in principal clinical manifestation and sex

Table 6: Principal clinical manifestation for *E. faecalis* and *E. faecium* bacteraemia, AGAR, 2022

Principal clinical manifestation	*E. faecalis* % (*n*)	*E. faecium* % (*n*)	Total % (*n*)	Significance*
Urinary tract infection	22.5 (171)	5.7 (33)	15.2 (204)	<0.01
No identifiable focus	16.3 (124)	10.0 (58)	13.6 (182)	<0.01
Intra-abdominal infection other than biliary tract	9.9 (75)	18.3 (106)	13.5 (181)	<0.01
Device-related infection without metastatic focus	9.5 (72)	15.9 (92)	12.2 (164)	<0.01
Biliary tract infection (including cholangitis)	7.9 (60)	17.1 (99)	11.9 (159)	<0.01
Febrile neutropenia	2.1 (16)	19.8 (115)	9.8 (131)	<0.01
Other clinical syndrome	8.9 (68)	8.6 (50)	8.8 (118)	ns
Endocarditis left-sided	13.7 (104)	0.7 (4)	8.1 (108)	<0.01
Skin and skin structure infection	2.6 (20)	1.7 (10)	2.2 (30)	ns
Osteomyelitis/septic arthritis	2.6 (20)	0.9 (5)	1.9 (25)	0.02
Device-related infection with metastatic focus	1.7 (13)	1.4 (8)	1.6 (21)	ns
Endocarditis right-sided	2.2 (17)	0.0 (0)	1.3 (17)	<0.01
Total	760	580	1,340	

ns = not significant
*Fisher's exact test for difference in principal clinical manifestation between *E. faecalis* and *E. faecium*

3.6. Length of hospital stay following bacteraemic episode

Information on length of hospital stay following bacteraemia was available for 1,441 (93.9%) enterococcal episodes.

Overall, 22.3% of patients remained in hospital for more than 30 days after blood culture collection (Table 7).

Table 7: Length of hospital stay following *Enterococcus* species bacteraemia, by vancomycin resistance and place of onset, AGAR, 2022

Species	Length of stay following bacteraemia				Total
	<7 days % (*n*)	7–14 % days (*n*)	15–30 % days (*n*)	>30 days % (*n*)	
All species	21.8 (314)	28.8 (415)	27.1 (390)	22.3 (322)	1,441
E. faecalis	21.8 (166)	29.6 (226)	26.1 (199)	22.5 (172)	763
vancomycin-resistant	–* (0)	–* (0)	–* (0)	–* (0)	0
vancomycin-susceptible	21.5 (163)	29.7 (225)	26.1 (198)	22.7 (172)	758
E. faecium	20.2 (116)	28.3 (163)	29.0 (167)	22.4 (129)	575
vancomycin-resistant	20.9 (56)	26.1 (70)	32.1 (86)	20.9 (56)	268
vancomycin-susceptible	19.1 (58)	30.4 (92)	26.7 (81)	23.8 (72)	303
Other *Enterococcus* species (*n* = 10)	31.1 (32)	25.2 (26)	23.3 (24)	20.4 (21)	103
Community onset					
E. faecalis	24.0 (125)	31.0 (161)	25.6 (133)	19.4 (101)	520
vancomycin-resistant	–* (0)	–* (0)	–* (0)	–* (0)	0
vancomycin-susceptible	23.8 (123)	30.9 (160)	25.7 (133)	19.5 (101)	517
E. faecium	30.0 (45)	32.0 (48)	26.0 (39)	12.0 (18)	150
vancomycin-resistant	22.6 (12)	30.2 (16)	35.8 (19)	11.3 (6)	53
vancomycin-susceptible	33.3 (32)	33.3 (32)	20.8 (20)	12.5 (12)	96
Hospital onset					
E. faecalis	16.9 (41)	26.7 (65)	27.2 (66)	29.2 (71)	243
vancomycin-resistant	–* (0)	–* (0)	–* (0)	–* (0)	0
vancomycin-susceptible	16.6 (40)	27.0 (65)	27.0 (65)	29.5 (71)	241
E. faecium	16.7 (71)	27.1 (115)	30.1 (128)	26.1 (111)	425
vancomycin-resistant*	20.5 (44)	25.1 (54)	31.2 (67)	23.3 (50)	215
vancomycin-susceptible*	12.6 (26)	29.0 (60)	29.5 (61)	29.0 (60)	207

* Insufficient numbers (<10) to calculate percentage

Note: vancomycin susceptibility not available for six *E. faecalis* (community [3]; hospital onset [3]) and four *E. faecium* (community [1]; hospital onset [3]).

3.7. Susceptibility testing results

The following sections present the results of susceptibility testing and the findings for AMR by place of onset and multi-drug resistance. Susceptibility testing methods are described in Appendix B.

Overall percentages of resistance or non-susceptibility using both CLSI breakpoints and EUCAST breakpoints are shown in Table 8. Resistance (as defined by EUCAST) by state and territory to glycopeptides in *E. faecium*, and high-level gentamicin resistance in *E. faecalis* is shown in Figure 2. Detailed resistance by state and territory can be found in Appendix C.

Two linezolid-resistant *E. faecium* from Victoria were confirmed. Both harboured the G2576T 23S rRNA mutation. One isolate with a linezolid MIC of >256 mg/L was ST2217, vancomycin resistant and harboured the *vanB* gene. The second isolate with a linezolid MIC of 8 mg/L was ST1424 and vancomycin susceptible.

Two daptomycin-resistant isolates from NSW, one *E. faecalis* and one *E. faecium* were confirmed. The *E. faecalis* with a daptomycin MIC of 8 mg/L was ST16 and harboured the F478L GdpD mutation[12]. The *E. faecium* with a daptomycin MIC of 24 mg/L was ST78 and harboured the A20D Cls mutation [13]. The daptomycin-resistant *E. faecium* was also vancomycin-resistant and harboured the *vanB* gene.

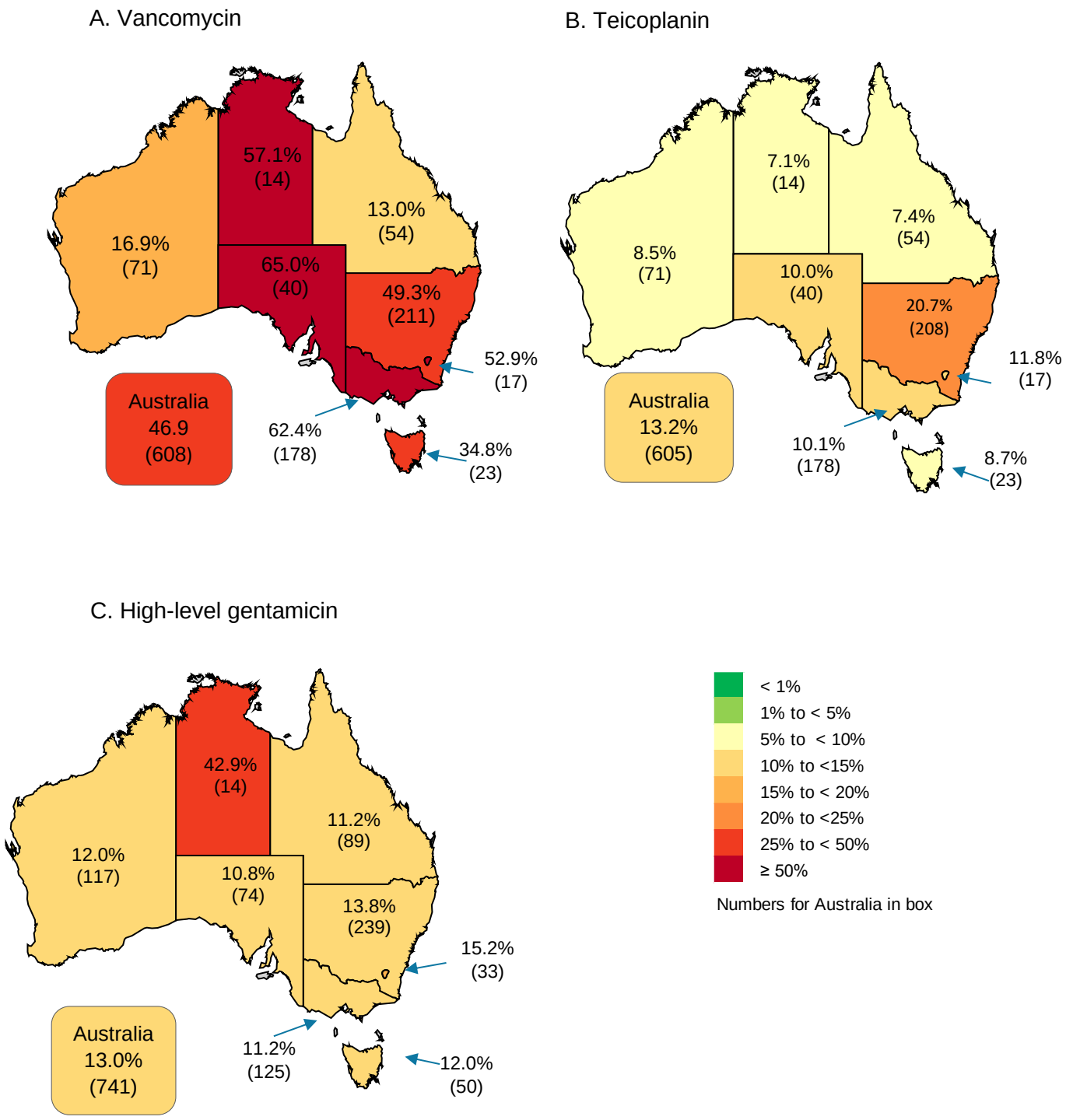
Table 8: Antimicrobial resistances for *E. faecalis* and *E. faecium* (CLSI and EUCAST), AGAR, 2022

Species and antimicrobial	Isolates (n)	CLSI		EUCAST	
		Intermediate % (*n*)	Resistant % (*n*)	Susceptible, increased exposure % (*n*)	Resistant % (*n*)
Enterococcus faecalis					
Ampicillin	807	–*	0.0 (0)	0.0 (0)	0.0 (0)
Benzylpenicillin	664	–*	0.9 (6)	–†	–†
Daptomycin	745	0.0 (0)	0.1 (1)	–†	–†
Linezolid	804	0.4 (3)	0.0 (0)	–*	0.0 (0)
Teicoplanin	807	0.0 (0)	0.0 (0)	–*	0.0 (0)
Vancomycin	807	0.0 (0)	0.0 (0)	–*	0.0 (0)
Enterococcus faecium					
Ampicillin	606	–*	95.4 (578)	0.5 (3)	95.4 (578)
Benzylpenicillin	480	–*	94.2 (452)	–†	–†
Daptomycin	58	0.0 (0)	1.7 (1)	–†	–†
Linezolid	607	0.3 (2)	0.3 (2)	–*	0.3 (2)
Teicoplanin	605	1.5 (9)	8.9 (54)	–*	13.2 (80)
Vancomycin	608	1.0 (6)	45.9 (279)	–*	46.9 (285)

CLSI = Clinical and Laboratory Standards Institute; EUCAST = European Committee on Antimicrobial Susceptibility Testing;

* No guidelines for indicated species
† No category defined

Figure 2: Percentage of *Enterococcus faecium* from patients with bacteraemia with resistance as defined by EUCAST to vancomycin (A) and teicoplanin (B), and *Enterococcus faecalis* with resistance to high-level gentamicin (C), Australia, AGAR, 2022



Antimicrobial resistance by place of onset

AMR (CLSI and EUCAST) in indicator species by place of onset, if known, are shown in Table 9.

Table 9: Antimicrobial resistances (CLSI, EUCAST), by place of onset, AGAR, 2022

Species and antimicrobial	Community onset					Hospital onset				
	No.	CLSI		EUCAST		No.	CLSI		EUCAST	
		% I	% R	% S-IEI	% R		% I	% R	% S-IE	% R
Enterococcus faecalis										
Ampicillin	541	–*	0.0	0.0	0.0	266	–*	0.0	0.0	0.0
Benzylpenicillin	451	–*	1.1	–†	–†	213	–*	0.5	–†	–†
Daptomycin	493	37.3	0.0	–†	–†	252	42.1	0.4	–†	–†
Linezolid	538	0.4	0.0	–*	0.0	266	0.4	0.0	–*	0.0
Teicoplanin	541	0.0	0.0	–*	0.0	266	0.0	0.0	–*	0.0
Vancomycin	541	0.0	0.0	–*	0.0	266	0.0	0.0	–*	0.0
Enterococcus faecium										
Ampicillin	155	–*	86.5	0.6	86.5	451	–*	98.4	0.4	98.4
Benzylpenicillin	120	–*	85.0	–†	–†	456	–*	97.2	–†	–†
Linezolid	156	0.6	0.0	–*	0.0	451	0.2	0.4	–*	0.4
Teicoplanin	155	1.9	8.4	–*	11.0	450	1.3	9.1	–*	14.0
Vancomycin	156	2.6	32.7	–*	35.3	452	0.4	50.4	–*	50.9

CLSI = Clinical and Laboratory Standards Institute; EUCAST = European Committee on Antimicrobial Susceptibility Testing; No. = number of isolates; I – Intermediate; R = Resistant; S-IE = susceptible, increased exposure.

* No guidelines for indicated species
† No category defined

3.8. Multi-drug resistance

Enterococci have expected resistant phenotypes to several antimicrobial classes and any additional acquired resistance severely limits the number of treatment options. The limited range of antimicrobials available on the test panels limits the ability to determine multiple acquired resistances in *E. faecalis* and *E. faecium*. Vancomycin-resistant enterococci are listed as a serious threat to public health[14] and have been identified as a major AMR threat in Australian healthcare facilities.[15]

3.9. PCR and whole genome sequencing

This section describes the results of the molecular epidemiology of *E. faecium* in the 2022 dataset. The benefits of molecular methods include increased accuracy in detecting the genetic mechanisms for AMR and clarifying the underlining epidemiology. Molecular methods also detect *van* genes in vancomycin variable enterococci which are vancomycin-susceptible enterococci harbouring *van* genes.

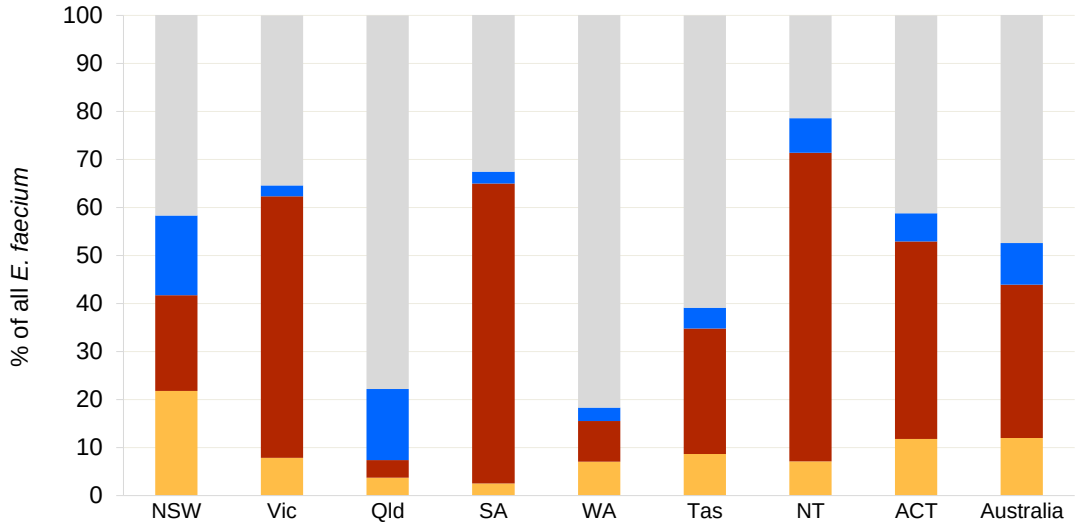
3.9.1. Molecular epidemiology of *Enterococcus faecium*

van genes

Results of PCR testing for *vanA* and *vanB* genes were available for 560 (91.4%) of the 613 *E. faecium* isolates. *van* genes were detected in 267/560 (47.7%) of *E. faecium*; *vanA* in 73 (13.0%) and *vanB* in 194 (34.7%) (Figure 3).

Where both vancomycin and *van* gene results were available for VREfm (n = 608, MIC > 4 mg/L), *vanA* was detected in 73/258 (28.3%) and *vanB* in 194/258 (72.1%). In 9/302 (3.0%) of vancomycin-susceptible *E. faecium*, *van* genes were detected: one with *vanA* and eight with *vanB*. All nine isolates had vancomycin MICs ≤ 4 mg/L.

Figure 3: Vancomycin genotype of *Enterococcus faecium* isolates, by state and territory, and nationally, AGAR, 2022



	NSW (n = 211)	Vic (n = 178)	Qld (n = 54)	SA (n = 40)	WA (n = 71)	Tas (n = 23)	NT (n = 14)	ACT (n = 17)	Australia (n = 608)
not vanA or vanB (n =293)	43.6	35.4	77.8	35.0	81.7	60.9	21.4	41.2	48.2
Not peformed (n = 48)	16.6	2.2	14.8	2.5	2.8	4.3	7.1	5.9	8.7
vanB (n =194)	19.9	54.5	3.7	62.5	8.5	26.1	64.3	41.2	31.9
vanA (n = 73)	21.8	7.9	3.7	2.5	7.0	8.7	7.1	11.8	12.0

Multi-locus sequence type

Of the 613 *E. faecium* isolates reported, 560 (91.4%) were available for typing by WGS (Table 10). Based on the MLST, 62 STs were identified. Overall, 85.2% of *E. faecium* were characterised into eight major STs (≥10 isolates): ST17 (*n* = 119); ST78 (*n* = 110); ST1424 (*n* = 81); ST796 (*n* = 50); ST80 (*n* = 45); ST1421 (*n* = 44), ST555 (n = 20) and ST117 (*n* = 10). There were 40 STs with a single isolate.

ST17 was the predominant ST in Queensland, Western Australia, and Tasmania. ST78 was predominant in the Australian Capital Territory, ST78 and ST555 in the Northern Territory. ST78 and ST796 were detected in equal numbers in Victoria, ST1424 was predominant in New South Wales, and ST555 in South Australia.

The distribution of vancomycin-resistant *E. faecium* STs across the Australian states and territories is shown in Figure 4.

Table 10: *Enterococcus faecium* MLST, by state and territory, AGAR, 2022

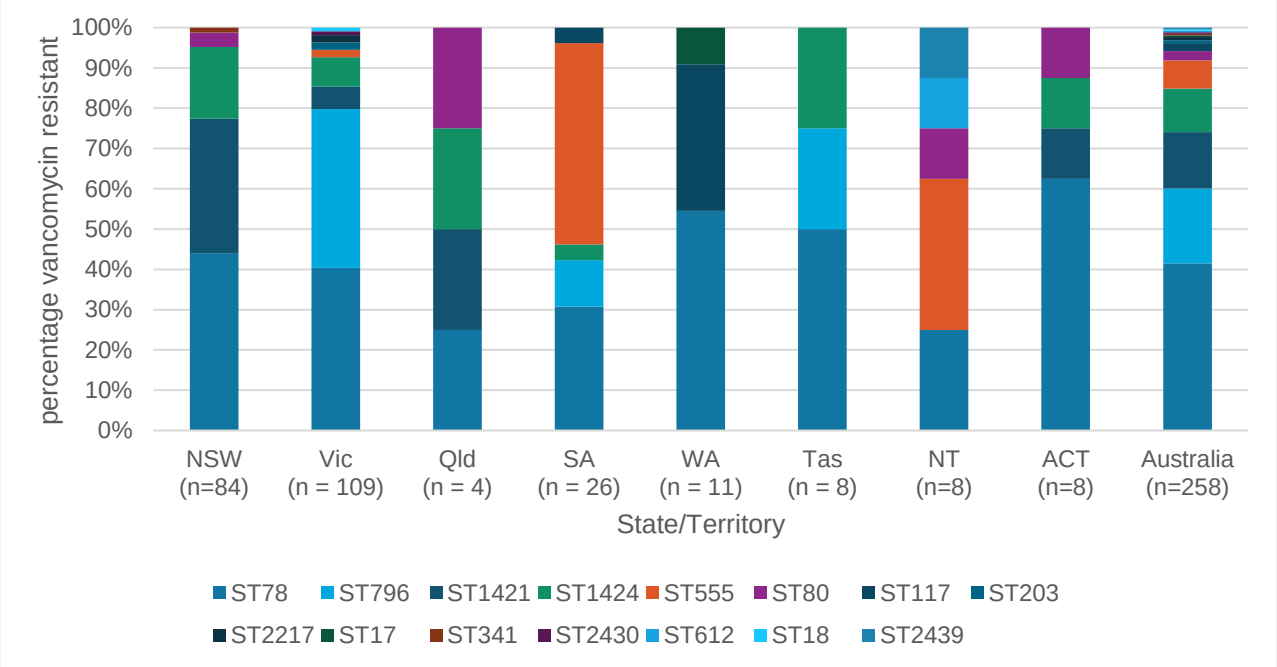
	Percentage, % (*n*)								
MLST	NSW	Vic	QLD	SA	WA	Tas	NT	ACT	Australia
ST17	8.3 (15)	14.9 (26)	52.2 (24)	17.5 (7)	52.2 (36)	40.9 (9)	7.7 (1)	6.3 (1)	21.3 (119)
ST78	21.1 (38)	25.3 (44)	2.2 (1)	20.0 (8)	8.7 (6)	18.2 (4)	23.1 (3)	37.5 (6)	19.6 (110)
ST1424	30.6 (55)	9.2 (16)	6.5 (3)	2.5 (1)	0.0 (0)	18.2 (4)	0.0 (0)	12.5 (2)	14.5 (81)
ST796	0.6 (1)	25.3 (44)	0.0 (0)	7.5 (3)	0.0 (0)	9.1 (2)	0.0 (0)	0.0 (0)	8.9 (50)
ST80	5.6 (10)	5.7 (10)	21.7 (10)	2.5 (1)	10.1 (7)	4.5 (1)	7.7 (1)	31.3 (5)	8.0 (45)
ST1421	18.3 (33)	4.0 (7)	6.5 (3)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	6.3 (1)	7.9 (44)
ST555	0.6 (1)	1.1 (2)	0.0 (0)	32.5 (13)	1.4 (1)	0.0 (0)	23.1 (3)	0.0 (0)	3.6 (20)
ST117	1.1 (2)	0.0 (0)	0.0 (0)	2.5 (1)	10.1 (7)	0.0 (0)	0.0 (0)	0.0 (0)	1.8 (10)
ST761	0.0 (0)	1.7 (3)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.5 (3)
ST538	1.7 (3)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.5 (3)
ST2220	0.0 (0)	0.0 (0)	4.3 (2)	0.0 (0)	0.0 (0)	0.0 (0)	7.7 (1)	0.0 (0)	0.5 (3)
ST203	0.0 (0)	1.1 (2)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	7.7 (1)	0.0 (0)	0.5 (3)
ST789	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	2.9 (2)	0.0 (0)	0.0 (0)	0.0 (0)	0.4 (2)
ST71	0.0 (0)	0.6 (1)	0.0 (0)	0.0 (0)	1.4 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.4 (2)
ST2217	0.0 (0)	1.1 (2)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.4 (2)
ST2201	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	2.9 (2)	0.0 (0)	0.0 (0)	0.0 (0)	0.4 (2)
ST1887	0.6 (1)	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.4 (2)
ST1693	0.0 (0)	0.0 (0)	4.3 (2)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.4 (2)
ST1283	1.1 (2)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.4 (2)
ST948	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST92	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST907	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST841	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.4 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST779	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)

MLST	Percentage, % (*n*)								
	NSW	Vic	QLD	SA	WA	Tas	NT	ACT	Australia
ST775	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST769	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST598	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.4 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST56	0.0 (0)	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST54	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST533	0.0 (0)	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST418	0.0 (0)	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST341	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST321	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.4 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST294	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.4 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST280	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST262	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST260	0.0 (0)	0.0 (0)	0.0 (0)	2.5 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST2440	0.0 (0)	0.0 (0)	0.0 (0)	2.5 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST2439	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	7.7 (1)	0.0 (0)	0.2 (1)
ST2438	0.0 (0)	0.0 (0)	2.1 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST2436	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.4 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST2435	0.0 (0)	0.0 (0)	0.0 (0)	2.5 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST2434	0.0 (0)	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST2433	0.0 (0)	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST2431	0.0 (0)	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST2430	0.0 (0)	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST2429	0.0 (0)	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST2428	0.0 (0)	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST2415	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	4.5 (1)	0.0 (0)	0.0 (0)	0.2 (1)
ST2226	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST22	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.4 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST2169	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST214	0.0 (0)	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST21	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST1984	0.0 (0)	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST192	0.0 (0)	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST19	0.0 (0)	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST127	0.6 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
ST1208	0.0 (0)	0.0 (0)	0.0 (0)	2.5 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.2 (1)
Total	**180**	**174**	**46**	**40**	**69**	**22**	**13**	**16**	**560**

MLST = multi-locus sequence type, ST = sequence type

* Insufficient numbers (<10) to calculate percentage

Figure 4: Distribution of vancomycin-resistant *Enterococcus faecium* sequence types, by state and territory, AGAR, 2022



MLST and *van* genes

The *vanA* gene was detected in six STs; ST17, ST1424, ST80, ST1421, ST117 and ST18.

The *vanB* gene was detected in 12 STs: ST17, ST78, ST1424, ST796, ST80, ST555, ST117, ST612, ST203, ST2217, ST341, and ST2439 (Table 11).

Table 11: Major *Enterococcus faecium* MLST harbouring *vanA* and/or *vanB* genes, AGAR, 2022

	Percentage* (*n*)				
MLST	***vanA***	***vanB***	***vanA* and *vanB***	***vanA* or *vanB* not detected**	**Total, *n***
ST17	0.8 (1)	2.5 (3)	0.0 (0)	96.6 (115)	119
ST78	0.0 (0)	100.0 (110)	0.0 (0)	0.0 (0)	110
ST1424	34.6 (28)	1.2 (1)	0.0 (0)	64.2 (52)	81
ST796	0.0 (0)	100.0 (50)	0.0 (0)	0.0 (0)	50
ST80	6.7 (3)	4.4 (2)	0.0 (0)	88.9 (40)	45
ST1421	81.8 (36)	0.0 (0)	0.0 (0)	18.2 (8)	44
ST555	0.0 (0)	90.0 (18)	0.0 (0)	10.0 (2)	20
ST117	40.0 (4)	10.0 (1)	0.0 (0)	50.0 (5)	10
Other types (*n* =54)	1.2 (1)	9.9 (8)	0.0 (0)	88.9 (72)	81
Total	13.0 (73)	34.6 (194)	0.0 (0)	52.3 (293)	560

MLST = multi-locus sequence type

* Percentage of total with *van* genes

3.10. Trend analysis (2013–2022)

Trend data were available for the period 2013 to 2022.

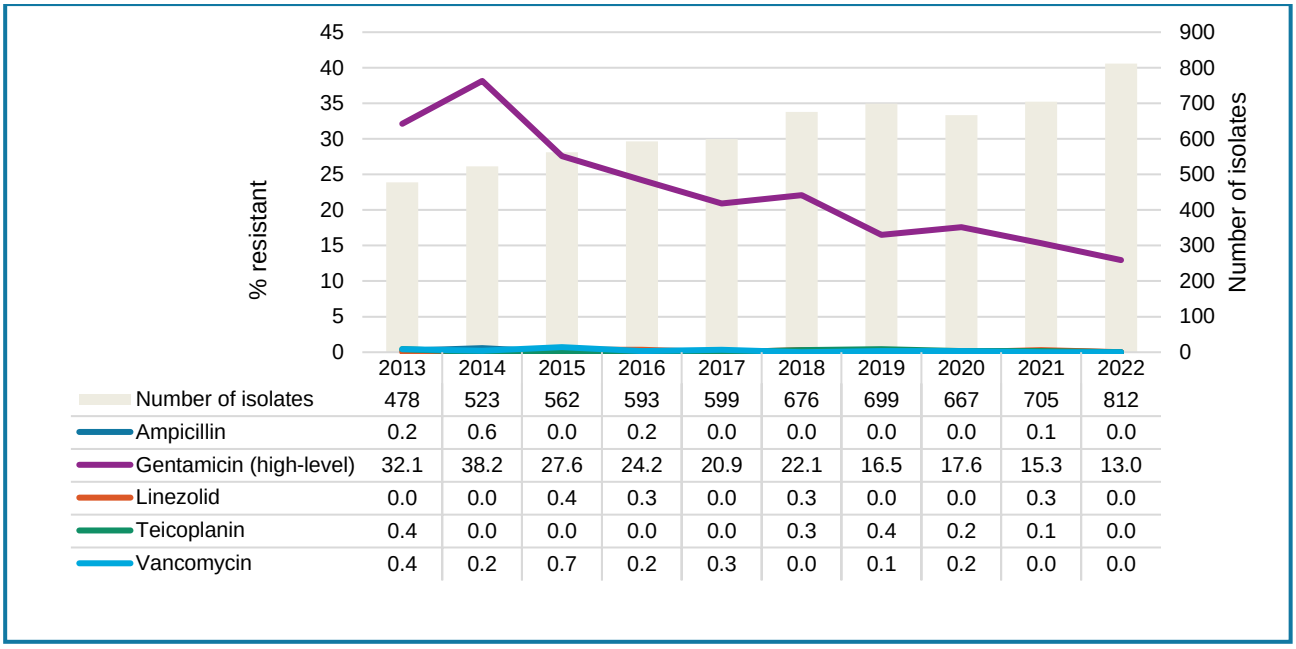
3.10.1. *Enterococcus* species

The 2022 program focused on the proportions of *E. faecium* and *E. faecalis* bacteraemia isolates demonstrating resistance to ampicillin, glycopeptides and other anti-enterococcal agents. Important trends for the period 2013–2022 are described below.

Enterococcus faecalis

National
Resistance (EUCAST) to key antimicrobial agents for *E. faecalis* over the ten-year period 2013 to 2022 is shown in Figure 5. Resistance to ampicillin, vancomycin, teicoplanin and linezolid remains rare. There has been a significant decreasing trend in high-level gentamicin resistance (X^2 for linear trend = 163.286, *P* =0.02)

Figure 5: *Enterococcus faecalis*, resistance (EUCAST), Australia, AGAR, 2013–2022



	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Number of isolates	478	523	562	593	599	676	699	667	705	812
Ampicillin	0.2	0.6	0.0	0.2	0.0	0.0	0.0	0.0	0.1	0.0
Gentamicin (high-level)	32.1	38.2	27.6	24.2	20.9	22.1	16.5	17.6	15.3	13.0
Linezolid	0.0	0.0	0.4	0.3	0.0	0.3	0.0	0.0	0.3	0.0
Teicoplanin	0.4	0.0	0.0	0.0	0.0	0.3	0.4	0.2	0.1	0.0
Vancomycin	0.4	0.2	0.7	0.2	0.3	0.0	0.1	0.2	0.0	0.0

EUCAST = European Committee on Antimicrobial Susceptibility Testing

Notes
1. Percentage resistance determined using EUCAST 2023 breakpoints for all years.
2. Number of contributors per year – 2013 and 2014, n = 27; 2015, n = 35; 2016, n = 33; 2017, n = 35, 2018, n = 38; 2019, n = 41, 2020, n = 42, 2021, n = 41, 2022, n = 43

State and territory
There were no significant changes in AMR among *E. faecalis* in 2022, compared to 2021.

Over the past five years (2018-2022), there was a significant decreasing trend in high-level gentamicin resistance in New South Wales (X^2 for linear trend = 4.256, *P* = 0.04), Victoria (X^2 for linear trend = 7.167, *P* =0.007), and the Australian Capital Territory (X^2 for linear trend = 6.369, *P* =0.01) (Table 12).

Table 12: *Enterococcus faecalis*, percentage resistant to gentamicin (high-level) (EUCAST) and number tested, state and territory, AGAR, 2013–2022

State and territory	Percentage resistant, (*n*) by year										Trend 2018–2022*
	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
New South Wales	40.0 (85)	42.4 (132)	29.3 (140)	28.2 (149)	16.7 (186)	24.2 (207)	15.3 (215)	19.0 (221)	19.8 (162)	13.8 (239)	▼
Victoria	34.0 (106)	38.7 (119)	27.4 (106)	21.9 (128)	19.8 (116)	23.1 (117)	22.2 (126)	24.8 (133)	16.0 (131)	11.2 (125)	▼
Queensland	27.6 (87)	34.3 (102)	25.5 (94)	28.6 (98)	21.4 (98)	16.3 (129)	13.0 (123)	9.3 (97)	9.0 (100)	11.2 (89)	↔
South Australia	31.6 (19)	35.3 (51)	28.1 (57)	29.4 (51)	35.5 (31)	23.6 (55)	9.4 (64)	13.8 (58)	17.4 (69)	10.8 (74)	↔
Western Australia	28.2 (71)	28.6 (63)	23.3 (90)	16.1 (87)	22.5 (89)	21.1 (90)	12.8 (78)	15.9 (88)	9.4 (106)	12.0 (117)	↔
Tasmania	18.2 (11)	30.8 (13)	25.0 (12)	14.8 (27)	20.0 (30)	16.1 (31)	12.2 (41)	7.4 (27)	9.1 (33)	12.0 (50)	↔
Northern Territory	† (6)	† (6)	40.0 (10)	† (7)	10.0 (10)	18.2 (11)	† (7)	† (5)	† (8)	42.9 (14)	↔
Australian Capital Territory	30.4 (23)	54.5 (33)	34.3 (35)	22.5 (40)	35.7 (28)	38.5 (26)	44.4 (36)	19.4 (31)	27.8 (36)	15.2 (33)	▼
Australia	32.1 (408)	38.2 (519)	27.6 (544)	24.2 (587)	20.9 (588)	22.1 (666)	16.5 (690)	17.6 (660)	15.3 (645)	13.0 (741)	▼

* Chi-squared test for trend for past five years (2018–2022), p-value <0.05, decrease ▼; ↔ no significant difference
† Not applicable, insufficient numbers (<10) to calculate percentage

Note: Percentage resistance determined using EUCAST 2023 breakpoints for all years.

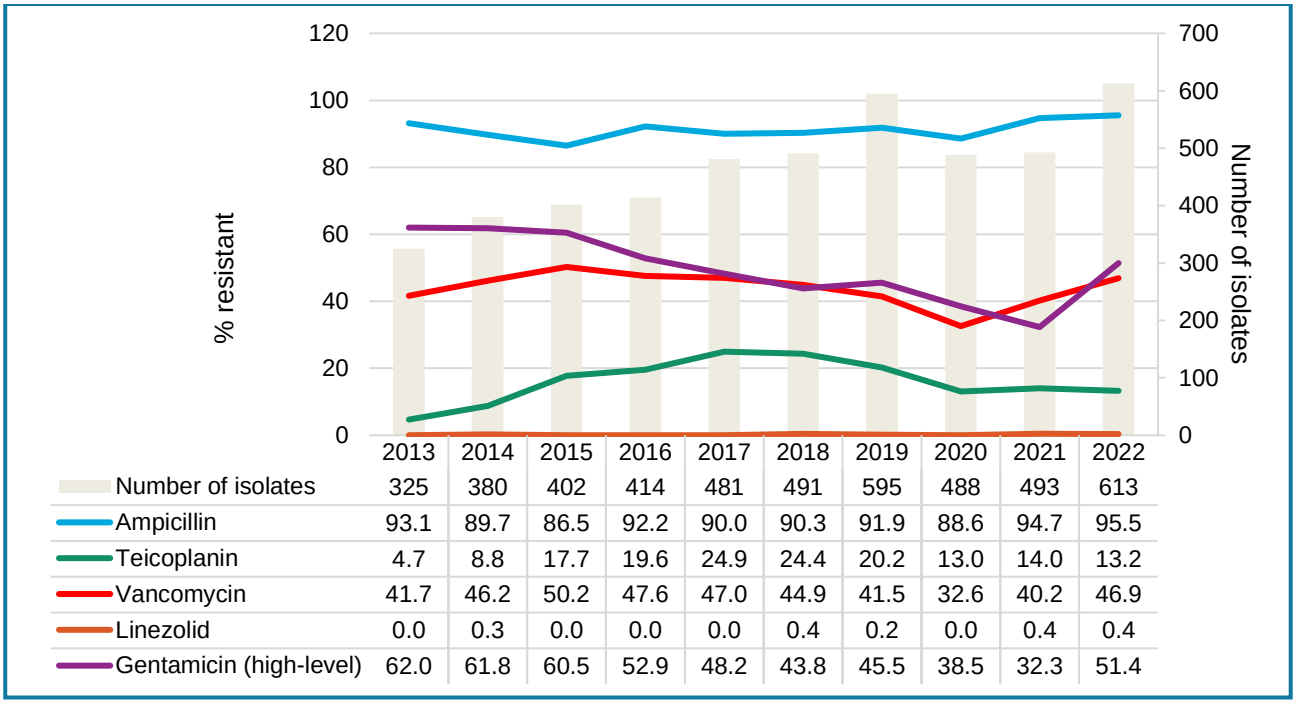
Enterococcus faecium

National

The total number of *E. faecium* isolated from patients with bacteraemia increased 15.8% in 2022 compared to 2021 (*n* = 523 in 2021; *n* = 613) (Figure 6). There was a significant increase in the proportion of *E. faecium* isolates resistant to vancomycin (*P* =0.03) but no significant change in teicoplanin resistance.

There was a significant increase in the proportion of *E. faecium* isolates resistant to gentamicin (high-level). The increase was seen in both vancomycin-resistant (52.0% in 2021, 92.1 in 2022), and vancomycin-susceptible (19.6% in 2021, 26.8% in 2022) *E. faecium* (Figure 7).

Figure 6: *Enterococcus faecium*, resistance (EUCAST), Australia, AGAR, 2013–2022



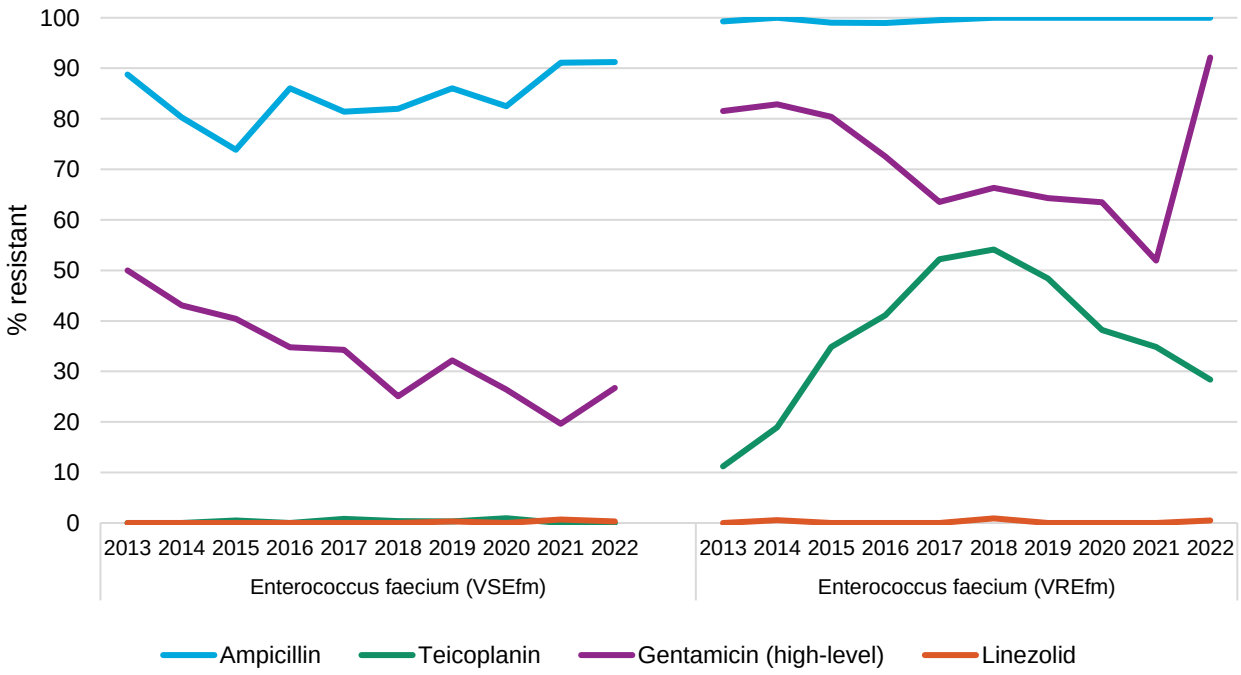
	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Number of isolates	325	380	402	414	481	491	595	488	493	613
Ampicillin	93.1	89.7	86.5	92.2	90.0	90.3	91.9	88.6	94.7	95.5
Teicoplanin	4.7	8.8	17.7	19.6	24.9	24.4	20.2	13.0	14.0	13.2
Vancomycin	41.7	46.2	50.2	47.6	47.0	44.9	41.5	32.6	40.2	46.9
Linezolid	0.0	0.3	0.0	0.0	0.0	0.4	0.2	0.0	0.4	0.4
Gentamicin (high-level)	62.0	61.8	60.5	52.9	48.2	43.8	45.5	38.5	32.3	51.4

EUCAST = European Committee on Antimicrobial Susceptibility Testing

Notes

1. Percentage resistance determined using EUCAST 2022 breakpoints for all years.
2. Number of contributors per year – 2013 and 2014, n = 27; 2015, n = 35; 2016, n = 33; 2017, n = 35, 2018, n = 38; 2019, n = 41, 2020, n = 42, 2021, n = 41, 2022, n = 43.

Figure 7: *Enterococcus faecium,* resistance (EUCAST), by vancomycin susceptibility, Australia, AGAR, 2013–2022



EUCAST = European Committee on Antimicrobial Susceptibility Testing; VSEfm = vancomycin susceptible *Enterococcus faecium*; VREfm = vancomycin resistant *Enterococcus faecium*

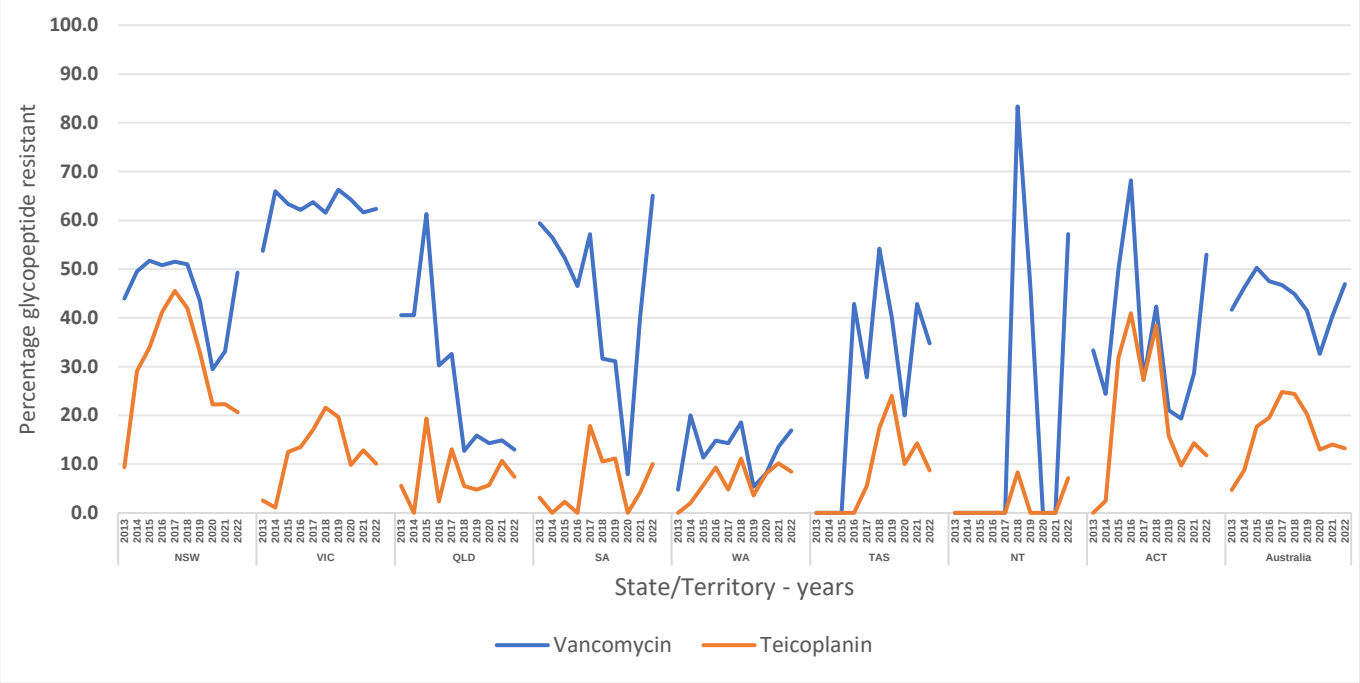
Notes

1. Percentage resistance determined using EUCAST 2022 breakpoints for all years.
2. Number of contributors per year – 2013 and 2014, n = 27; 2015, n = 35; 2016, n = 33; 2017, n = 35, 2018, n = 38; 2019, n = 41, 2020, n = 42, 2021, n = 41, 2022, n =43.

State and territory

The proportion of glycopeptide-resistant *E. faecium* by state and territory is shown in Figure 8. Nationally, the proportion of VREfm increased from 198/492, 40.2% in 2021 to 285/608, 46.9% in 2022) . The increase was notable in South Australia (19/47, 40.4% in 2021 to 26/40, 65.0% in 2022, P < 0.01). Teicoplanin resistance in *E. faecium* was stable (69/492, 14.0% in 2021 to 80/605, 13.2% in 2022).

Figure 8: *Enterococcus faecium*, glycopeptide resistance (EUCAST), by state and territory, and nationally, AGAR, 2013–2022



Notes

1. Percentage resistance determined using EUCAST 2022 breakpoints for all years.
2. Number of contributors per year – 2013 and 2014, n = 27; 2015, n = 35; 2016, n = 33; 2017, n = 35, 2018, n = 38; 2019, n = 41, 2020, n = 42, 2021, n = 41, 2022, n = 43.
3. Insufficient numbers (< 10) to calculate percentage for Tasmania (2013–2015) and the Northern Territory (2013-2016).

The only significant trend in vancomycin resistance in *E. faecium* over the past five years (2018-2022) was an increase in South Australia (X^2 for linear trend = 10.29, *P* <0.01) (Table 13). Over the same period, teicoplanin resistance in *E. faecium* decreased significantly in New South Wales (X^2 for linear trend = 23.11, *P* < 0.01), Victoria (X^2 for linear trend = 10.568, *P* <0.01), the Australian Capital Territory (X^2 for linear trend = 5.306, *P* = 0.02) and Australia overall (X^2 for linear trend = 29.944, *P* < 0.01) (Table 14).

Table 13: *Enterococcus faecium*, percentage resistant to vancomycin (EUCAST) and number tested, state and territory, AGAR, 2013–2022

State and territory	Percentage resistant, (*n*) by year										Trend 2018–2022*
	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
New South Wales	43.9 (107)	49.5 (103)	51.7 (116)	50.8 (124)	51.5 (167)	51.0 (151)	43.5 (209)	29.4 (180)	33.1 (139)	49.3 (211)	↔
Victoria	53.8 (80)	66.0 (94)	63.3 (120)	62.2 (111)	63.7 (135)	61.5 (130)	66.3 (163)	64.2 (123)	61.6 (164)	62.4 (178)	↔
Queensland	40.5 (37)	40.5 (37)	61.3 (31)	30.2 (43)	32.6 (46)	12.7 (55)	15.9 (63)	14.3 (35)	14.9 (47)	13.0 (54)	↔
South Australia	59.4 (32)	56.5 (46)	52.3 (44)	46.5 (43)	57.1 (28)	31.6 (38)	31.1 (45)	7.9 (38)	40.4 (47)	65.0 (40)	▲
Western Australia	4.8 (42)	20.0 (50)	11.3 (53)	14.8 (54)	14.3 (63)	18.5 (54)	5.4 (56)	8.1 (62)	13.6 (59)	16.9 (71)	↔
Tasmania	† (5)	† (7)	† (8)	42.9 (14)	27.8 (18)	54.2 (24)	40.0 (25)	20.0 (10)	42.9 (14)	34.8 (23)	↔
Northern Territory	† (3)	† (1)	† (8)	† (4)	† (5)	83.3 (12)	46.2 (13)	† (6)	† (8)	57.1 (14)	↔
Australian Capital Territory	33.3 (18)	24.4 (41)	50.0 (22)	68.2 (22)	27.3 (22)	42.3 (26)	21.1 (19)	19.4 (31)	28.6 (14)	52.9 (17)	↔
Australia	41.7 (324)	46.2 (379)	50.2 (402)	47.5 (415)	46.7 (484)	44.9 (490)	41.5 (593)	32.6 (485)	40.2 (492)	46.9 (608)	↔

* Chi-squared test for trend for past five years (2018–2022), p-value <0.05, decrease ▼; ↔ no significant difference
† Not applicable, insufficient numbers (<10) to calculate percentage

Note: Percentage resistance determined using EUCAST 2023 breakpoints for all years.

Table 14: *Enterococcus faecium*, percentage resistant to teicoplanin (EUCAST) and number tested, state and territory, AGAR, 2013–2022

State and territory	Percentage resistant, (*n*) by year										Trend 2018–2022*
	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
New South Wales	13.0 (69)	31.4 (70)	29.9 (77)	38.0 (71)	46.7 (92)	36.1 (83)	26.3 (99)	14.9 (74)	23.9 (71)	22.1 (77)	▼
Victoria	2.5 (80)	1.1 (94)	12.5 (120)	13.5 (111)	17.0 (135)	21.5 (130)	20.7 (150)	10.4 (115)	15.2 (125)	11.5 (139)	▼
Queensland	6.5 (31)	0.0 (34)	20.0 (30)	2.5 (40)	13.6 (44)	6.3 (48)	5.4 (56)	5.7 (35)	10.6 (47)	7.4 (54)	↔
South Australia	3.1 (32)	0.0 (44)	2.3 (43)	0.0 (43)	17.9 (28)	10.5 (38)	11.6 (43)	0.0 (32)	4.3 (47)	10.0 (40)	↔
Western Australia	0.0 (31)	2.4 (42)	3.3 (30)	6.1 (33)	10.0 (30)	13.9 (36)	2.9 (35)	8.3 (36)	7.9 (38)	10.0 (50)	↔
Tasmania	#N/A (5)	#N/A (7)	#N/A (8)	#N/A (3)	#N/A (7)	#N/A (6)	21.4 (14)	#N/A (5)	#N/A (7)	8.3 (12)	↔
Northern Territory	#N/A (3)	#N/A (1)	#N/A (6)	#N/A (4)	#N/A (2)	#N/A (8)	#N/A (9)	#N/A (5)	#N/A (4)	7.7 (13)	↔
Australian Capital Territory	0.0 (16)	2.4 (41)	31.8 (22)	40.9 (22)	27.3 (22)	38.5 (26)	15.8 (19)	9.7 (31)	14.3 (14)	11.8 (17)	▼
Australia	5.2 (267)	7.5 (333)	15.8 (336)	16.5 (327)	23.9 (360)	21.6 (375)	16.9 (425)	9.6 (333)	13.6 (353)	12.4 (402)	▼

* Chi-squared test for trend for past five years (2018–2022), p-value <0.05, bold text significant decrease ▼; ↔ no significant difference
† Not applicable, insufficient numbers (<10) to calculate percentage

Note: Percentage resistance determined using EUCAST 2023 breakpoints for all years.

Glycopeptide-resistance and *van* gene trends in *Enterococcus faecium*

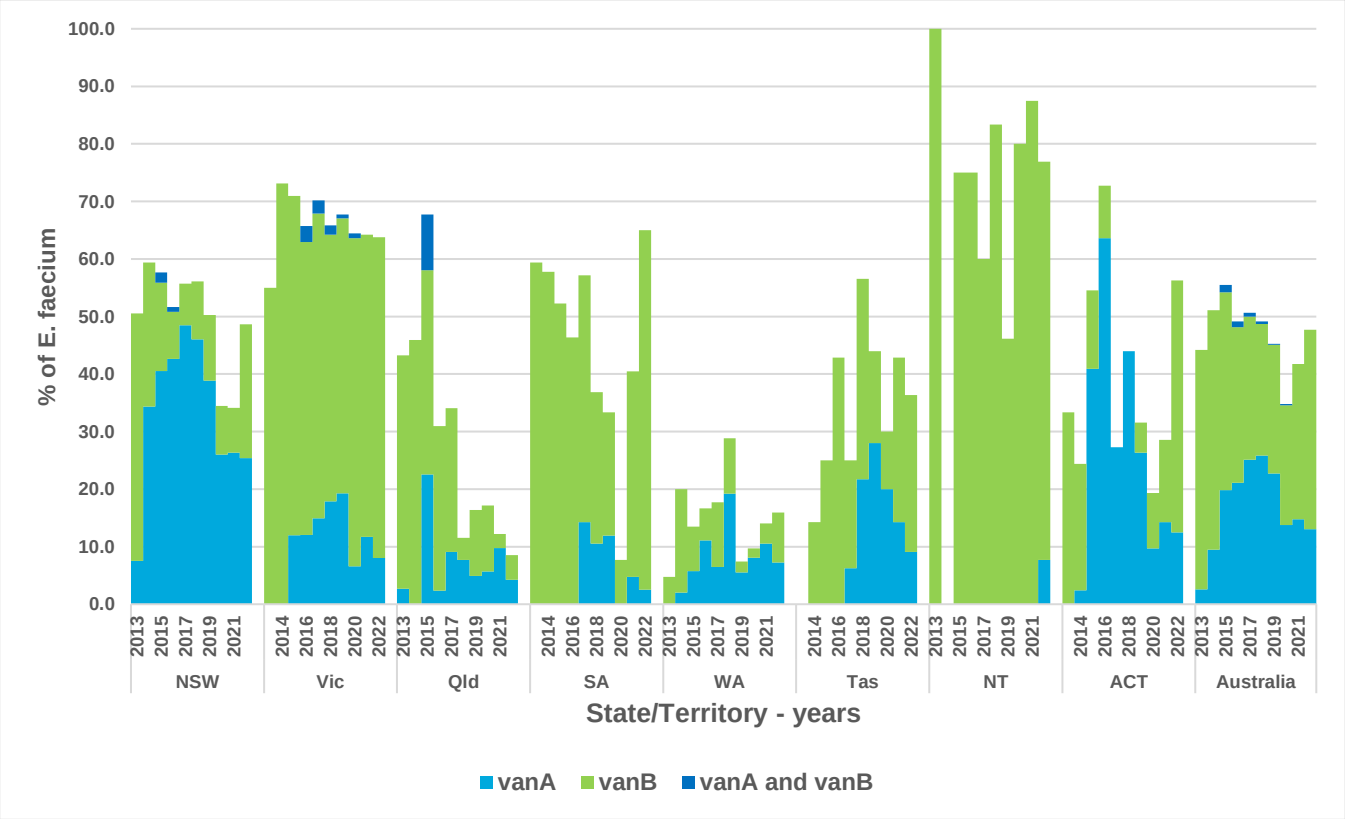
In 2022, glycopeptide resistance was predominantly due to the *vanB* gene. Overall, the proportion of *vanA E. faecium* in 2022 remained stable compared to 2021. The proportion of *vanB E. faecium* increased from 27.0% in 2021 to 34.7% in 2022 (P = 0.02) .

There was a significant increase in *vanB E. faecium* in New South Wales in 2022 from (10/129, 7.8%) in 2021, to (42/181, 23.2%) in 2022. However, 34 *E. faecium* were not sent for testing in 2022 which may have influenced the resistance rate.

Over the past five-year period (2018-2022) there was a significantly decreasing trend in *vanA* genes in New South Wales (X^2 for linear trend, 19.8773, P <0.01), Victoria (X^2 for linear trend, 10.1728, P = 0.001), South Australia (X^2 for linear trend, 3.8404, P = 0.05), the Australian Capital Territory (X^2 for linear trend, 7.7857, P =0.01) and Australia overall, (X^2 for linear trend, 38.3565, P <0.01). Over the same period there was a significant increase in *van*B genes in South Australia, (X^2 for linear trend14.3117, P =0.01, the Australian Capital Territory, (X^2 for linear trend, 15.2965, P <0.01) and in Australia overall, (X^2 for linear trend, 23.4895, P <0.01).

There is considerable variation in the proportion of *E. faecium* with *van* genes by state and territory, and the *van* type (Figure 9).

Figure 9: Proportion of *van* genes in *Enterococcus faecium* by state and territory, and nationally, AGAR, 2013–2022



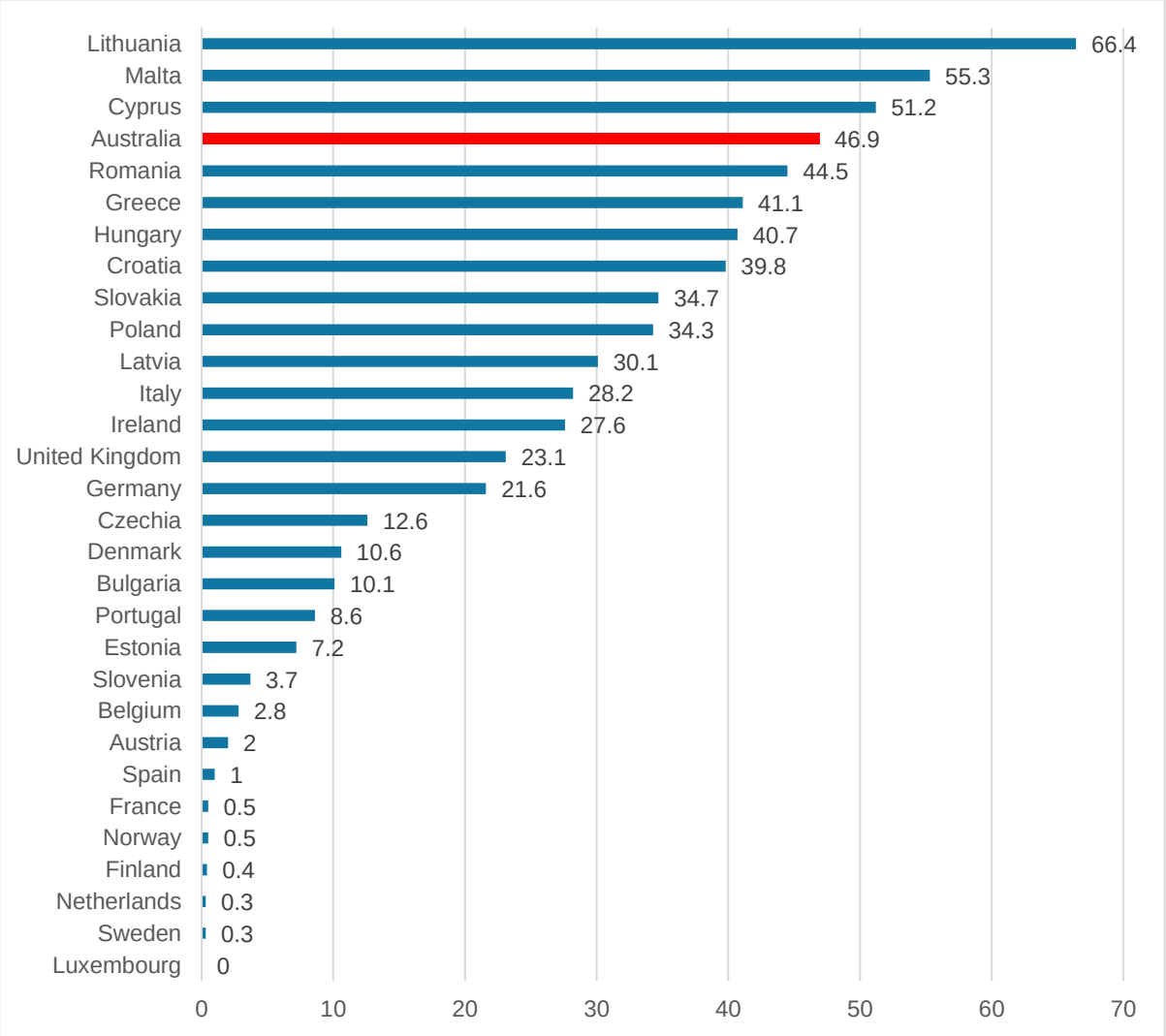
4. International comparisons

Data from AGAR can be compared with data from the European Antimicrobial Resistance Surveillance Network (EARS-Net) program[16], and the World Health Organization (WHO) Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR) network[17], as all these surveillance systems review resistance in bacterial pathogens isolated from blood cultures.

EARS-Net is based on routine clinical antimicrobial susceptibility data from local and clinical laboratories reported to ECDC by appointed representatives from the Member States. The data originate form national AMR surveillance initiatives and/or laboratory networks. Only data from invasive isolates (blood and cerebrospinal fluid) are included in EARS-Net.

Australia ranks in the top third in rates of resistance to vancomycin in *E. faecium* compared to the thirty participating European countries (Figure 10), ranking fourth. In 2021, 2020, 2019, 2018 Australia ranked eighth, tenth, fourth, and second respectively.

Figure 10: Comparison of *Enterococcus faecium* rates of resistance to vancomycin in Australia and European countries, blood culture isolates, AGAR, 2022



EU/EEA = European Union (EU) and European Economic Area (EEA) countries population-weighted mean percentages

Source: EARS-Net (Europe)[18], CAESAR (United Kingdom)[17]

5. Limitations of the study

Although this study is considered comprehensive in its coverage of Australia, and the methods follow international standards, the data and their interpretation have a number of limitations:

- The data are not denominator controlled, and there is currently no consensus on an appropriate denominator for such surveys; hospital size, patient throughput, patient complexity and local antibiotic use patterns all influence the types of resistance that are likely to be observed.
- Although data have been collected from 55 hospitals across Australia, it is not clear how representative the sample is of Australia as a whole, because the proportion of the population that is served by the laboratories that participate in AGAR is not accurately known. Further, it is likely that the proportion of the population served differs in each state and territory
- Concentration ranges of some antimicrobial agents in both the Vitek® and Phoenix™ cards limit the ability to accurately identify 'susceptible' for some combinations of antimicrobial agents and species.
- Data are classified into hospital- and community-onset infections; healthcare-associated community-onset infections may be included in the community-onset group.

6. Discussion and conclusions

AGAR data show that in 2022 episodes of enterococcal bacteraemia episodes in Australia had their onset overwhelmingly in the community. For the AESOP, the most frequent predisposing clinical manifestations were urinary tract infection, biliary tract, and intra-abdominal infection. However, episodes where there was no identifiable focus also contributed to high proportions of presentations for enterococcal bacteraemia overall.

E. faecium bacteraemia has significant clinical consequences and resource implications, due to increased length of hospital stay. Bacteraemia episodes contributed to increased length of hospital stay; the average length of stay in all Australian public hospitals in 2018–2019 was 5.5 days.[19] Thirty-day all-cause mortality due to *E. faecium* in 2022 was 26.9% (CO, 30.5%; HO, 25.7%); there was a significant difference in 30-day all-cause mortality between vancomycin-susceptible and resistant episodes (19.4% and 34.4% respectively $P < 0.01$)

In the 2022 survey, 47.0% of *E. faecium* harboured *vanA* or *vanB* genes; in 2020 it was 39.6%. Vancomycin, which until recently was the mainstay of therapy for *E. faecium*, can no longer be recommended empirically; agents with less certain efficacy such as linezolid are the alternative.

For almost two decades, and unlike in most other countries where vancomycin resistance is a problem, vancomycin resistance in Australia was dominated by the *vanB* genotype. However, in the 2018 survey, 52.4% of vancomycin-resistant *E. faecium* bacteraemias were due to *vanA*: increasing from 6.1% in 2013. In 2019 the *vanA* genotype numbers started to decline (48.5%) in 2020 - 36.4%, 2021 - 36.0%. In the 2022 survey 27.7% of VREfm bacteraemia harboured the *vanA* gene.

The percentage of *E. faecium* bacteraemia isolates that are resistant to vancomycin in Australia is significantly higher than that seen in almost all European countries. Australia ranks in the top third in rates of resistance to vancomycin in *E. faecium* (46.9%), ranking fourth highest. In 2021 it was ranked eighth highest; and in 2020, tenth highest.[17, 18]

The percentage of high-level gentamicin resistance in *E. faecium* has increased significantly from 2021 to 2022 ($P < 0.01$). This increase was seen in both vancomycin-susceptible and vancomycin-resistant isolates ($P = 0.05$ and 0.01 respectively). This was driven by the increase in ST1421, ST1424 and ST78 clones, in particular in NSW and the addition of one hospital in NSW that had not participated in 2021.

Although infection prevention and control strategies are essential for control of this organism, many antimicrobials have been implicated in the development of vancomycin non-susceptible *E. faecium.* Vancomycin, used commonly as an empiric therapeutic choice for MRSA, and other broad-spectrum antibiotics which select for enterococci due to intrinsic resistance, especially the third-generation cephalosporins, are widely used in Australia.

It should be noted, outbreaks of multi-drug resistant organisms occur in hospitals and other institutional care settings, and substantial transmission occurs before invasive blood stream infections develop. AGAR data may therefore underestimate local or regional spread of multidrug-resistant organisms and may not assist with early detection of sentinel resistances. AGAR bacteraemia data need to be assessed with other sources of information to provide broader insights into antimicrobial resistance in Australia. The AURA Surveillance System enables these assessments via Australian Passive AMR Surveillance (APAS) and National Alert System for Critical Antimicrobial Resistances (CARAlert) data, which complement AGAR data.

AGAR surveillance remains core to Australia's response to the problem of increasing AMR. AGAR data contribute to understanding AMR in Australian human health settings, and to informing the national response to AMR.

Abbreviations

Abbreviation	Term
AGAR	Australian Group on Antimicrobial Resistance
AMR	Antimicrobial resistance
APAS	Australian Passive AMR Surveillance
ASA	Australian Society for Antimicrobials
AURA	Antimicrobial Use and Resistance in Australia
CARAlert	National Alert System for Critical Antimicrobial Resistance
CI	Confidence interval
CLSI	Clinical and Laboratory Standards Institute
CO	Community-onset
EUCAST	European Committee on Antimicrobial Susceptibility Testing
HO	Hospital-onset
MDR	Multi-drug resistant
MIC	Minimum inhibitory concentration
MLST	Multi-locus sequence type
PCR	Polymerase chain reaction
ST	Sequence type
VREfm	Vancomycin-resistant *Enterococcus faecium*
VSEfm	Vancomycin-susceptible *Enterococcus faecium*
WGS	Whole genome sequencing
WHO	World Health Organization

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Participating members of AGAR:

Hospital	AGAR members
Alfred Hospital, Vic	Adam Jenney and Jacqueline Williams
Alice Springs Hospital, NT	James McLeod
Austin Hospital, Vic	Marcel Leroi and Elizabeth Grabsch
Canberra Hospital, ACT	Peter Collignon and Susan Bradbury
Children's Hospital Westmead, NSW	Alison Kesson and Andrew Jarrett
Concord Hospital, NSW	Thomas Gottlieb and John Huynh
Dandenong Hospital, Vic	Tony Korman and Kathryn Cisera
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Gosford Hospital, NSW	Gabrielle O'Kane and Nola Hitchick
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John Hunter Hospital, NSW	Hemalatha Varadhan and Bree Harris
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Royal Perth Hospital, WA	Owen Robinson and Geoffrey Coombs
Royal Prince Alfred Hospital, NSW	Sebastiaan van Hal and Thomas Le
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Reference laboratories

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Appendix A. Study design

Fifty-five institutions participated in the 2022 survey, forty-eight adult and seven children's hospitals. All states and territories were represented. The hospital peer group/type[20] represented were:

Principal referral hospitals (*n* = 27)
Public acute group A hospitals (*n* = 5)
Children's hospitals (*n* = 6)
Combined Women's and children's hospitals (*n* = 1)
Private acute group A hospitals (*n* = 2)
Private acute group B hospitals (*n* = 1)
Regional and district hospitals from north-west regional Western Australia (*n* = 13)

- Public acute group C hospitals (*n* = 5)
- Public acute group D hospitals (*n* = 6)
- Very small hospitals (*n* = 2)

The thirty-three laboratories that serviced the hospitals participating in AGAR collected all isolates from different patient episodes of enterococcal bacteraemia. In patients with more than one isolate, a new episode was defined as a new positive blood culture more than two weeks after the initial positive culture.

An episode was defined as community onset if the first positive blood culture was collected ≤48 hours after admission, and as hospital onset if collected >48 hours after admission.

All laboratories that participated in AGAR obtained basic laboratory information for each patient episode plus varying demographic information, depending on the level at which they are enrolled in the program. There are two levels of enrolment: Bronze and Silver (Tables A1). At Bronze level, participating laboratories provided date of collection, date of birth, sex, postcode, and admission date. At Silver level, participating laboratories provided discharge date, device-related infection, principal clinical manifestation, outcome at seven and 30 days, and date of death if appropriate.

Table A1: Level of AESOP participation of hospitals that contributed data on enterococcal bacteraemia, by state and territory, 2022

State or territory	Number of hospitals	Level of participation	
		Bronze	Silver
New South Wales	13	2	11
Victoria	8	0	8
Queensland	7	0	7
South Australia	3	0	3
Western Australia	19*	2	21
Tasmania	2	0	2
Northern Territory	2	1	1
Australian Capital Territory	1	0	1
Total	55	5	50

*includes 13 regional and district hospitals in north-western Australia

Appendix B. Methods

Species identification

Isolates were identified using the routine methods for each institution. These included the Vitek® and Phoenix™ automated microbiology systems, and, if available, mass spectrometry (MALDI - TOF).

Susceptibility testing

Testing was performed using two commercial semi-automated methods: Vitek 2 (bioMérieux) (*n* = 31) and Phoenix (BD) (*n* = 3), which are calibrated to the ISO (International Organization for Standardization) reference standard method of broth microdilution. Commercially available Vitek 2 (AST-P612 or AST-P643) or Phoenix (PMIC-84) cards were used by all participants throughout the survey period.

The CLSI M100[9] and the EUCAST v13.1[10] breakpoints from January 2023 were used in the analysis.

Additional tests performed on *E*. faecalis and *E. faecium* include:

- E-test MIC if:
  - Linezolid MIC >4 mg/L, or if MIC not provided
  - Daptomycin MIC > 4 mg/L
  - Vancomycin and teicoplanin if MIC not provided or discrepant with *van* gene
  - Ampicillin > 8 mg/L (*E. faecalis*) or ampicillin ≤ 4 mg/L (*E. faecium*), or if MIC not provided
- *van* gene PCR on *E. faecalis* if:
  - Vancomycin MIC > 4 mg/L or teicoplanin > 2 mg/L and *van* gene not provided.

Clinical and outcome data

Device related infection

Device-related bacteraemia is defined as a bacteraemia derived from central (which includes portacaths, PICC lines) or peripheral (venous and arterial) intravascular devices, from catheter-associated urinary tract infection (including nephrostomy tubes and stents), or ventilator-associated respiratory tract infection or bacteraemias associated with biliary stents.

Principal clinical manifestation

For AESOP surveys, the principal clinical manifestation for each patient episode is categorised as:

- Biliary tract infection (including cholangitis)
- Device-related infection with metastatic focus
- Device-related infection without metastatic focus
- Endocarditis Left-sided
- Endocarditis Right-sided
- Febrile neutropenia
- Intra-abdominal infection other than biliary tract
- No identifiable focus
- Osteomyelitis/septic arthritis
- Other clinical syndrome
- Skin and skin structure infection
- Urinary tract infection

Length of hospital stay following bacteraemia
Length of hospital stay following bacteraemia is calculated from the date of blood culture collection to patient discharge or death.

All-cause mortality
All-cause mortality refers to outcome (died, survived, unknown) at 7- and 30-days from blood culture date of collection.

Antimicrobials tested

The antimicrobials tested are shown in Table B1.

Table B1: Antimicrobials on susceptibility testing cards and interpretive guidelines for CLSI and EUCAST for *Enterococcus* species

Antimicrobial agent	Breakpoint (mg/L)						
	CLSI M100*				EUCAST v13.0†		
	S	SDD	I	R	S, SD	S, IE	R
Benzylpenicillin	≤8		–§	≥16	–#	–#	–#
Amoxicillin–clavulanic acid**	–#		–#	–#	≤4	8	>8
Ampicillin	≤8		–§	≥16	≤4	8	>8
Daptomycin							
Enterococcus faecium		≤4	–	≥8	–#	–#	–#
Enterococcus spp. other than *E. faecium*	≤2		4	≥8	–#	–#	–#
Doxycycline (Phoenix™ card)	≤4		8‡	≥16‡	–#	–#	–#
Erythromycin	≤0.5		1–4	≥8	–#	–#	–#
Imipenem (Phoenix™ card)	–#		–#	–#	≤0.001	0.002–4	>4
Linezolid	≤2		4	≥8	≤4	–§	>4
Quinupristin-dalfopristin							
Enterococcus faecium §§	≤1		2	≥4	≤1	**–§**	**>1**
Rifampicin	≤1		2	≥4	–#	–#	–#
Teicoplanin	≤8		16	≥32	≤2	–§	>2
Vancomycin	≤4		8–16	≥32	≤4	–§	>4

CLSI = Clinical and Laboratory Standards Institute; EUCAST = European Committee on Antimicrobial Susceptibility Testing; I = intermediate (CLSI); R = resistant; S = susceptible (CLSI); S, IE = susceptible, increased exposure (EUCAST); S, SD = sensitive, standard dosing (EUCAST); SDD = sensitive dose dependent (CLSI)

Note: Information in **blue** boldface type is new or modified since 2022.

* The breakpoints selected to identify resistance are described in the *Performance Standards for Antimicrobial Susceptibility Testing.* 33rd *ed. CLSI supplement* M100, 2023
† EUCAST breakpoint tables for interpretation of MICs and zone diameters, version 13.1, 2023 (www.eucast.org)
§ No category defined
# No guidelines for indicated species
** Clavulanate concentration fixed at 2mg/L
‡ The concentration range available on the current Phoenix™ card restricts the ability to identify intermediate and resistant categories
§§ CLSI breakpoints for vancomycin-resistant *E. faecium* only

Molecular confirmation of resistance

For *E. faecium* WGS was performed by the Antimicrobial Resistance Infectious Diseases (AMRID) Research Laboratory at Murdoch University using the Illumina NextSeq™ 500 platform. The Nullarbor bioinformatic pipeline[21] was used to identify the multi-locus sequence type and *van* gene.

Quality control

Quality control strains used were those recommended by CLSI and EUCAST standards.

Data validation

Various checks were made to ensure that the data were valid. These included:

- Null values in the mandatory fields
- Missing MIC data
- Patient age if ≥100 or <0 days
- Confirm dates when:
  - Specimen collected after patient discharged or died
  - Patient discharged or died before admitted
  - Patient admitted before born
  - Patient admitted more than two days after specimen collected
  - Patient admitted more than six months before specimen collected

Appendix C. Susceptibility to antimicrobial agents

Overall percentages of resistance or non-susceptibility for *E. faecium* and *E. faecalis* are shown in Table C1. For some antimicrobials, the concentration range tested did not distinguish between intermediate susceptibility (I) and resistant (R), and the term non-susceptible (NS) was used to describe these isolates.

Table C1: Susceptibility (CLSI and EUCAST) to antimicrobial agents in *E. faecium* and *E. faecalis* by state and territory, 2022

Antimicrobial agent and species	Category*	CLSI and EUCAST percentage susceptibility at indicated category								
		NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
Ampicillin										
Enterococcus faecalis	n	245	180	91	75	118	51	14	33	807
	%R	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Enterococcus faecium	n	201	171	53	36	65	23	13	16	578
	%R	95.7, 95.7	96.1, 96.1	98.1, 98.1	90.0, 90.0	91.5, 91.5	100.0, 100.0	100.0, 100.0	94.1, 94.1	95.4, 95.4
Benzylpenicillin										
Enterococcus faecalis	n	223	101	89	74	118	12	14	33	664
	%R	1.3, –†	1.0, –†	1.1, –†	0.0, –†	0.8, –†	0.0, –†	0.0, –†	0.0, –†	0.9, –†
Enterococcus faecium	n	199	81	54	39	70	7	13	17	480
	%R	94.5, –†	96.3, –†	98.1, –†	84.6, –†	92.9, –†	n/a	92.3, –†	94.1, –†	94.2, –†
Daptomycin										
Enterococcus faecalis	n	246	179	91	44	117	22	14	32	745
	%R	0.4, –†	0.0, –†	0.0, –†	0.0, –†	0.0, –†	0.0, –†	0.0, –†	0.0, –†	0.1, –†
Enterococcus faecium	n	39	0	0	17	2	0	0	0	58
	%R	2.6, –†	n/a	n/a	0.0, –†	n/a	n/a	n/a	n/a	1.7, –†
Linezolid										
Enterococcus faecalis	n	244	179	90	75	118	51	14	33	804
	%R	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.8	0.0, 0.0	0.0, 0.0	0.0, 3.0	0.0, 0.2
Enterococcus faecium	n	211	177	54	40	71	23	14	17	607
	%R	0.0, 0.0	1.1, 1.1	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.3, 0.3
Teicoplanin										
Enterococcus faecalis	n	245	180	91	75	118	51	14	33	807
	%R	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Enterococcus faecium	n	208	178	54	40	71	23	14	17	605
	%R	13.0,	6.7,	5.6,	7.5,	7.0,	4.3,	7.1,	11.8,	8.9,

Antimicrobial agent and species	Category*	CLSI and EUCAST percentage susceptibility at indicated category								
		NSW	Vic	Qld	SA	WA	Tas	NT	ACT	Australia
		20.7	10.1	7.4	10.0	8.5	8.7	7.1	11.8	13.2
Vancomycin										
Enterococcus faecalis	n	245	180	91	75	118	51	14	33	807
	%R	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0	0.0, 0.0
Enterococcus faecium	n	211	178	54	40	71	23	14	17	608
	%R	48.8, 49.3	60.1, 62.4	13.0, 13.0	65.0, 65.0	16.9, 16.9	30.4, 34.8	57.1, 57.1	52.9, 52.9	45.9, 46.9

CLSI = Clinical and Laboratory Standards Institute; ECOFF = epidemiological cut-off value; EUCAST = European Committee on Antimicrobial Susceptibility Testing; I = intermediate (CLSI) or susceptible, increased exposure (EUCAST); n/a = insufficient numbers (<10) to calculate; NS = intermediate plus resistant; R = resistant; SDD = sensitive dose dependent (CLSI)

* Category analysed for each organism. If different for CLSI and EUCAST, they are separated by a comma.

† No breakpoints defined for indicated species